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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,647	12/10/2001	Carl Johan Friddle	LEX-0284-USA	3815

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,647	FRIDDLE ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5,6,8,9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 5-6,8-9, 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 04 March 2005 has been entered in full. Claims 5-6, 8, and 11 are amended. Claims 1-2, 4, 7, and 10 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 3, 5-6, 8-9, and 11 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the specification as set forth at pg 3 of the previous Office Action (01 November 2004) is *withdrawn* in view of the new title (04 March 2005).

2. The rejection of claims 1, 3, and 5-11 under 35 U.S.C. § 101 as set forth at pg 3-7 of the previous Office Action (01 November 2004) is *withdrawn in part* in view of cancelled claims 1, 7, and 10 (04 March 2005).

3. The rejection of claims 1, 3, and 5-11 under 35 U.S.C. § 112, first paragraph (enablement) as set forth at pg 7-13 of the previous Office Action (01 November 2004) is *withdrawn in part* in view of the cancelled claims and the amended claims which no longer recite polynucleotide fragments or variants (04 March 2005).

4. The rejection of claims 1, 6, and 9 under 35 U.S.C. § 112, first paragraph (written description) as set forth at pg 13-15 of the previous Office Action (01 November 2004) is *withdrawn* in view of the amended claims which no longer recite polynucleotide fragments or variants (04 March 2005).

5. The rejection of claims 1, 6, and 9 under 35 U.S.C. §102(e), as set forth at pg 15-16 of the previous Office Action (01 November 2004) is *withdrawn* in view of the amended claims (04 March 2005).

Information Disclosure Statement

Any references which the Applicant wishes for the Examiner to review and make of record should be supplied in the form of an Information Disclosure Statement pursuant to 37 C.F.R. § 1.98(a)(1) which requires a list of all patents, publications, or other information submitted for consideration by the Office. Submission of the proper PTO-1449 form with copies of the references listed therein will be taken into due consideration by the Examiner. In the response of 04 March 2005, Applicant provided numerous references, including an English language abstract for document DE 19841413C. However, no new PTO-1449 form was provided.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

6. Claims 3, 5-6, 8-9, and 11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth for the claims at pg 3-7 of the previous Office Action (01 November 2004).

Specifically, claims 3, 5-6, 8-9, and 11 are directed to an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2 and an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

The claims also recite recombinant expression vectors and a host cell comprising the expression vector.

Applicant's arguments (04 March 2005), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the claimed sequence has clearly been described in the specification as an ion channel protein, and more particularly a voltage-gated potassium channel protein. Applicant argues that the claimed sequence shares 100% identity at the amino acid level over the entire length of SEQ ID NO: 2 with two sequences that are present in Genbank, which have been annotated by independent third party scientists unaffiliated with Applicant as "Homo sapiens voltage-gated potassium channel subunit Kv10.1a" and "Homo sapiens potassium voltage-gated channel subfamily G, member 3" (Accession Nos. AF454547 and NM_172344, respectively). Applicant also contends that three independent groups of scientists have established that the claimed sequence specifically interacts with the well-studied Kv2.1 voltage-gated potassium channel subunit to form functions voltage-gated potassium ion channels (Sano et al., FEBS Lett 512: 230-234, 2002; Ottschytsch et al. Proc Natl Acad Sci USA 99:7986-7991, 2002; Vega-Saenz de Miera, Brain Res Mol Bran Res 123 : 91-103, 2004). Applicant states that these references are evidence that other skilled artisans have confirmed the assertion that the claimed sequence is a voltage-gated potassium ion channel protein.

Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner acknowledges that the polynucleotide of SEQ ID NO: 21 of the instant application is 100% similar to the polynucleotide of Vega-Saenz de Miera and 50.6% similar to the polynucleotide of Sano et al. and Ottschytsch et al. However, the instant specification, the prior

art, and post-filing date art do not teach any significance or functional characteristics of the human polynucleotide (SEQ ID NO: 1) or polypeptide (SEQ ID NO: 2). It is a matter of law that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. The fact that some experimentation is required to establish the physiological role of the novel human protein (NHP) of the instant application simply confirms that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form. The state of the art also reports that potassium channels constitute the most diverse class of ion channels with respect to kinetic properties, regulation, pharmacology, and structure (pg 1329; Lehmann-Horn et a. Physiol Rev 79 (4): 1317-1372). Over 50 distinct channels have been identified in humans in both excitable and non-excitable cell types. The channels are involved in the control of a variety of cellular functions, including neuronal firing, cellular proliferation, and neurotransmitter and hormone secretion (pg 7887, ¶ 1; Chavez et al. J Biol Chem 274(12): 7887-7892, 1999). Therefore, one skilled in the art would not know the utility and function of the claimed NHP polynucleotide of SEQ ID NO: 2, even if it was a putative voltage-gated potassium channel because, as discussed in the related art above, potassium channels include a wide range of biologically active channels, and neither the prior art nor the specification provides for the physiological significance of the disclosed and claimed channel.

It is also noted that the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the

specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

It is clear from the instant specification that the human NHP polypeptide encoded by the claimed polynucleotide is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and

substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an Applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a nucleic acid encoding a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein, the instant invention is incomplete. In the absence of knowledge of the natural substrate or biological significance of this protein, there is no immediately obvious patentable use for it. Since the instant specification does not disclose a "real world" use for Kir5.1 then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

(ii) Applicant contends that the claimed sequence is described in the specification as a voltage-gated ion channel protein that is involved in high blood pressure, arrhythmia, and diabetes (pg 13, lines 19-22). Applicant also argues that the sequence has been shown to modulate Kv2.1 voltage-gated potassium ion channel subunits and that the association of Kv2.1 voltage-gated potassium ion channel subunits and high blood pressure, arrhythmia, and diabetes were all well-known in the art at the time the application was filed. Applicant cites references in Exhibits G-K for support.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the specification only states, "a genomic library can be constructed using DNA obtained from an individual suspected of carrying, or known to carry, a mutant NHP allele (e.g., a person manifesting a NHP-associated phenotype such as, for example, obesity, high blood pressure, connective tissue disorders, infertility, diabetes, alopecia, arrhythmia, etc.)" (pg 13, lines 17-22). The NHP gene and polypeptide of the instant application have *not* been associated with any disease or disorder, nor have they been shown to be predictive of such. The specification, the prior art, and post-filing date art do not demonstrate a specific nexus between the claimed polynucleotide of SEQ ID NO: 1 of the instant application any disease or disorder. The specification does not disclose the tissues or cell types the polynucleotide is normally and/or abnormally in. The specification also discloses nothing about the normal levels of expression of the polynucleotide. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

(iii) Applicant asserts that the Examiner's position directly contradicts the position of the USPTO itself, as set forth in Example 10 of the Revised Interim Utility Guidelines Training Materials, which clearly establishes that structural similarity can be used to establish function, and thus establish a particular utility.

Applicant's arguments have been fully considered but are not found to be persuasive. Example 10 is inapposite to the facts of the instant case. The polynucleotide sequence in Example 10 of the Utility Guidelines has high homology to DNA ligase encoding nucleic acids. In this example, DNA ligases have a well-established utility in the art based on this class of protein's ability to ligate DNA. However, the polynucleotide and polypeptide of the instant application are not supported by a specific and asserted utility or a well established utility although Applicant asserts that the polypeptide of SEQ ID NO: 2 encoded by the claimed polynucleotide of SEQ ID NO: 1 is homologous to the existing voltage-gated potassium channels. However, a function of the NHP of SEQ ID NO: 2 is not demonstrated. Also, the literature discloses many DNA ligases which have been fully characterized at the structural and functional levels. In the instant case, there is only similar post-filing date proteins and polynucleotides, which have not been fully characterized functionally.

(iv) At pages 8-11, Applicant submits that the present invention has a number of additional substantial and credible utilities, not the least of which is in forensic biology, as described in the specification at pg 3, line 12. Applicant argues that at pg 17, lines 3-5, a coding single nucleotide polymorphism was identified at position 432 of SEQ ID NO: 1, (specifically, a silent

G/C polymorphism) which can result in a glycine being present at amino acid position 144 of SEQ ID NO: 2. Applicant states that such polymorphisms are the basis for forensic analysis.

Applicant's arguments have been fully considered but are not found to be persuasive. The use of polymorphisms is not specific to any disease or disorder or characteristic known to be useful for forensics. The asserted use in forensics is a use for any polymorphism and is not specific. Asserted uses for chromosome mapping, arrays, and forensics are not specific and are useful for any polymorphisms. As such, the disclosed use of the polymorphism is not different than the use of any other polymorphism., The specification does not disclose what the polymorphism is specific for and how this specificity would be useful in forensic analysis. Applicant argues that correlation of the polymorphism for a specific disease or disorder in not the standard for usefulness under 35 U.S.C. § 101. This again is not persuasive. Applicant has not provided a specific use for the polymorphism. It is a generic use that is applicable to any polymorphism and not specific for the disclosed polymorphism. As such, the sequence does not meet the "specific" prong of the utility analysis as set forth in the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001. Applicant argues that the population can at least distinguish 50% of individuals for the other half. This is not found to be persuasive. Applicant has not kept in mind that humans have two copies of each gene and therefore the argument is based on genetics that are not particular to humans. Applicant argues that even in the worst case scenario, that it would distinguish 50% of the individuals and that polymorphisms have been used in forensic analysis for decades and that it is clearly a real world utility. Forensic analysis can be performed on the basis of restriction length

polymorphisms, but the specification does not describe restriction length polymorphisms. The specification does not teach any forensic technique that uses a single nucleic acid polymorphism other than an allegation of use to parse a population and as such has a real world utility. The specification does not teach any population analysis for the nucleic acid/amino acid polymorphism and as such, the skilled artisan would have to perform population analyses to identify or reasonably confirm a "real world" context of use because none of the restriction length markers useful in forensic analysis currently parse only 50% of the population. Applicants argue that polymorphisms are used in paternity testing and to identify or rule out suspects in criminal cases. This is not persuasive because any single polymorphism is not useful in determining paternity, nor has Applicant demonstrated that a single polymorphism is so useful. The use of the polymorphism is not presented in a manner or in a "real world" context because the population distribution is not known and not taught and therefore, the value of the polymorphism in combination with others is not taught by the specification. The use of polymorphisms is complicated by the population dynamics and human genetics. The specification sets forth none of the particulars as to how the alleged polymorphism is useful in a real world manner. Without population distribution data, there can be no use in forensics. It is clear that this need for further characterization of the polymorphism and its distribution indicates that the polymorphism has not been described in the specification in a manner that is consistent with a substantial utility. Applicant cites relevant case law at pg 10 of the response, however, it is noted that Applicant's polymorphism necessarily requires expectations of further research as set forth above.

(v) Applicant cites *In re Brana* (34 USPQ2d 1436 (Fed. Cir. 1995) and argues that the statement of utility in the specification must be accepted, unless one skilled in the art would have reason to doubt the objective truth of such a statement.

Applicant's arguments have been fully considered but are not found to be persuasive. Although as discussed in *In re Brana*, 34 USPQ 1436 (Fed. Cir. 1995), that pharmaceutical inventions necessarily include further research and development, it is clear from the instant specification that the polypeptide described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility.

(vi) Applicant asserts that given the association between the presently claimed sequence and high blood pressure, arrhythmia, and diabetes, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins. Applicant submits that the specification describes how the sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Applicant states that DNA chips have utility, as evidence by hundreds of issued U.S. patents. Applicant argues that evidence of the real world substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Applicant asserts that the real world substantial industrial utility of gene sequences appears to be widespread and well established. Applicant also contends that given the widespread utility of "gene chip" methods using public domain gene sequence information, there can be little doubt that the use of the presently claimed novel and medically relevant sequences would have great utility in such DNA chip applications. Finally, Applicant states that the present sequences are specific markers of the human genome and such specific markers are targets for the discovery of drugs that associated with human disease and those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using DNA chips.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification does not teach the skilled artisan any diseases or conditions associated with a mutated, deleted, translocated, upregulated, or downregulated gene of the instant application (SEQ ID NO: 1). Significant further experimentation would be required of one skill in the art to identify such a disease or condition. Furthermore, whereas a scale or a microarray or a gas

chromatograph has patentable utility as a research tool, the objects being evaluated with those research tools do not necessarily have patentable utility. In the instant case, the claimed polynucleotide is not disclosed as having a specific activity, or having any property (such as a differential pattern of expression in diseased tissue) that can be specifically useful. The claimed invention is, in fact, the object of further study, merely inviting further research. Moreover, use of the claimed polypeptide in an array for screening purposes is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicant's individual polynucleotide is affected by, for example, a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this polynucleotide could be put.

Additionally, commercial success requires more than the mere sale of a compound. Commercial success of genomic data is not necessarily evidence of patentable utility. Commercial success is discussed in the MPEP at 716.03 and appears to be applicable to obviousness rejections, but does not appear to be a valid consideration for utility which requires specific, substantial and credible utility. Applicant also has not established a nexus between the *claimed* invention and evidence of commercial success. Applicant's argument is also not persuasive because sale of a compound is not evidence of commercial success and sale of a

compound for use as a scientific tool does not appear to be a specific, substantial and credible utility as set forth in the "REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS".

Applicant cites Carl Zeiss Stiftung v. Renishaw PLC, 945 F.2d 1173, 20 USPQ2d 1094 (Fed. Cir. 1991) which sets forth that "an invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications". However, Carl Zeiss is inapposite to the facts of the instant case. In Carl Zeiss, the district court had found that a claim to a probe containing a stylus which is mounted to a movable arm above a table which supports an object to be measured lacked utility because "the arbitrary presentation of part of an invention does not constitute a claim of a valid invention" and that the claimed device could not function as a probe. See Carl Zeiss at 1180. In the instant case, the claims lack utility not because they are incomplete, and not because they do not set forth the best or only way to accomplish a result, and not because they are not unique, but because they do not have either a well-established utility or a specific and substantial asserted utility. First, Applicant is mischaracterizing the Examiner's position regarding the requirements for a specific utility. There is no dispute on the case law itself. The issue at dispute is what constitutes a specific utility. A specific utility is a utility specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. To satisfy the utility requirement under 35 U.S.C. §101, a utility does not need to be unique; however, it must be specific. The use of the present nucleic acid in tracking gene expression patterns on a gene chip is not specific, because such a use would be applicable to any nucleic acids. Further, the specification does not disclose a specific DNA target. The asserted

patentable utility of a chromosomal marker or to detect chromosomal aberrations for the claimed NHP nucleic acid molecules is not substantial because one skilled in the art would not readily use the nucleotide sequences since they are not associated with a specific disease-related gene. As noted above, such uses are all considered research uses only designed to identify a particular function of the claimed molecules and are not a substantial utility. Thus, all asserted uses are not specific and substantial.

It is further noted that the patents on batteries, automobile tires, golf balls, and treatments for a variety of human diseases are issued by the USPTO because the invention in each patent has a specific and substantial utility, not simply because the claimed subject matter is related to batteries, automobile tires, golf balls, or disease treatment. For example, a golf ball has a specific feature that makes the ball fly higher and further away as compared with other balls; a compound has a particular property that can be used to treat a specific disease, e.g., prostate cancer. Such is not the case here.

While the Examiner agrees with the Applicant on the scientific value of the claimed polynucleotide sequences and on the significance of expressed sequence information in structural analysis of genomic data, such a use of the claimed polynucleotide sequence in gene mapping does not represent a specific and substantial utility. The Venter et al. publication cited by the Applicant merely shows that the significance of expressed sequences in the structural analysis of genomic data; they do not show that the present polynucleotide sequence has a patentable utility.

(vii) At pg 18 of the Response, it has been indicated that while Applicant is well aware of the new Utility Guidelines set forth by the USPTO, it has been long established that the current rules regarding the examination on patent applications is and always has been the patent laws set forth

in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination as set forth by the USPTO. It is stated that Applicant is unaware of any significant recent changes in either 35 U.S.C. § 101 or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. Applicant contends that this is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do no comply with the new Utility Guidelines.

Applicant's arguments have been fully considered but are not found to be persuasive. It is noted that Applicant challenges the legality of the Patent Examination Utility Guidelines. Since an Examiner has no authority to comment on the legality of the Guidelines, this issue must be reserved for ruling by the Board of Patent Appeals and Interferences. The current rejection is in compliance with the most currently-published version of the Utility Guidelines which require that all biological inventions must have credible, specific and substantial ("real world") utility. Additionally, each Patent Application is examined on its own merits. The invention that was deemed allowable in one patent has no bearing on this application.

7. Claims 3, 5-6, 8-9, and 11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pg 7 of the previous Office Action (01 November 2004).

Applicant's arguments (04 March 2005) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the above-mentioned reasons.

Applicant argues that the concerns for 35 USC §112, first paragraph have been addressed in the arguments made for 35 USC §101.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, since Applicant has not provided evidence to demonstrate that the claimed nucleic acid molecules have a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

8. Claims 9 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or cultured cell comprising an expression vector, does not reasonably provide enablement for a host cell comprising an expression vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Examiner has interpreted the claims as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy. The basis for this rejection is set forth for claims 9-11 at pg 10-13 of the previous Office Action (01 November 2004).

Applicant's arguments (04 March 2005) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the above-mentioned reasons.

(i) Regarding the Examiner's argument that no methods or working examples are disclosed in the specification for transgenic animals and gene therapy with the claimed NHP gene,

Applicant states that it has long been established that "there is no statutatory requirement for the disclosure of a specific example" (*In re Gay*, 309 F.2d 769, 135 USPQ 311 (CCPA, 1962).

Applicant's arguments have been fully considered but are not found to be persuasive. A specification may lack a working example, but the specification must provide sufficient guidance so that one skilled in the art can practice the claimed invention without undue experimentation. Although the fact pattern of *In re Gay* (which discusses the sufficiency of disclosure for a rice cooking container) is slightly different than that of the instant rejection (transgenic animals and gene therapy), the U.S. Court of Customs and Patent Appeals states that the "Essence of first portion of first paragraph of 35 U.S.C. 112 is that specification shall disclose an invention in such a manner as will enable one skilled in the art to make and utilize it". Although Applicant need not to have actually reduced the invention to practice prior to filing the application, the lack of a working example is only one factor to be considered, especially in a case involving an unpredictable art (MPEP § 2164.02). The specification of the instant application at pg 2 and 16-19 only outlines prophetic procedures (not working examples) for expression of the NHP gene in transgenic animals and for gene therapy. However, this is not adequate guidance, but is merely an invitation for the artisan to use the current invention as a starting point for further experimentation. The skilled artisan must resort to trial and error experimentation to generate transgenic animals and to deliver the NHP gene of SEQ ID NO: 1 to target tissues in a subject. As was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166

USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991).

(ii) Regarding the Examiner's argument concerning the unpredictability in the art with making transgenic animals, Applicant indicates the state of the art with regard to making transgenic animals as of the filing date of the present application (December 2001). Applicant argues that there are numerous examples of transgenic worms, mice, rats, rabbits, guinea pigs, pigs, birds, goats, and monkeys, years prior to the filing date of the present application and cites several references as Exhibits Z-NN). Applicant also asserts that all that is required in order to satisfy the enablement requirement is making any transgenic animal, not the perfect transgenic animal. Applicant submits that the large number of reports in the literature on a variety of transgenic animals strongly argues against such a use requiring "undue experimentation". Applicant cites *In re Nelson*, 126 USPQ 242 (CCPA 1960); *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968), and *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976).

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, while numerous transgenic animals have been made to date, the use of the animal remains an issue because the phenotype, the overall outcome, remains highly unpredictable. Factors as obscure as the genetic background of the animal can mean success or failure of getting the desired expression to lead to the phenotypic outcome. As supported by the art made of record in the previous Office Action (01 November 2004), this art remains very unpredictable. While the unpredictability alone can be enough to raise reasonable doubt as to the enablement of

the claimed invention (*In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)), this is but one of the factors relied upon in making the rejection.

Additionally, a specification may be enabling even though some experimentation is necessary, but the amount of experimentation, however, must not be unduly extensive. According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed". Additionally, as was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). Regarding the instant application, in view of the lack of guidance provided by the specification for identifying and isolating embryonal cells which can contribute to the germ line of any non-human mammal other than the mouse, such as dogs or cows, the skilled artisan would not have had a reasonable expectation of success in generating any and all non-human transgenic animals using ES cell technology.

(iii) Regarding the Examiner's argument concerning gene therapy, Applicant contends that there are a number of reports in the literature, prior to the filing date of the present application, concerning a variety of gene therapy vectors and successful gene therapy regimes. Applicant states that even if further experimentation might be required in certain aspects of the present invention, this does not preclude a finding that the invention is enabled. Applicant cites *In re*

Brana, 34 USPQ 1436 (Fed. Cir. 1995) and *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976).

Applicant's arguments have been fully considered but are not found to be persuasive. The successes in the gene therapy art have been limited and very specific. The design of the vector, the method of targeting, and the host responses all remain critical factors in designing a successfully gene therapy protocol. The instant specification does not overcome these obstacles. The guidance provided in the specification does not specifically address any of these factors. Overall, gene therapy remains unpredictable as supported by the art cited by the Examiner in the previous Office Action of 01 November 2004.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate a transgenic animal expressing the NHP protein and to introduce and express a NHP nucleic acid in a cell of an organism for therapy, the lack of direction/guidance presented in the specification regarding how to introduce a NHP nucleic acid in the cell of an organism to be able produce that NHP, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of making transgenic animals and the unpredictability of transferring genes into an organism's cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated host cell...").

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
02 June 2005

ELIZABETH C. KEMMERER
PRIMARY EXAMINER